Specification

Please amend paragraph 49 on page 15 as follows;

[0049] The chemogenomic response can be obtained by any available means, for example by employing a panel of reporter cells, each group of cells having a reporter gene operatively connected to a different selected regulatory region. Alternatively, one can employ primary tissue isolates, cells or cell lines lacking reporter genes, and can determine the expression of a plurality of genes directly. Direct detection methods include direct hybridization of mRNA with oligonucleotides or longer DNA fragments such as cDNA or even fragments of cloned genomic DNA (whether in solution or bound to a solid phase), reverse transcription followed by detection of the resulting cDNA, Northern blot analysis, and the like. One can employ target amplification methods (for example, PCR amplification of cDNA using Taqman® polymerase, and other enzymatic methods) and/or signal amplification methods (for example, employing highly-labeled probes, chromogenic enzymes, and the like). Polynucleotide probe arrays for expression monitoring can be made and used according to any techniques known in the art. See for example, D. J. Lockhart, et al., Nature Biotechnol (1996) 14:1675-80; G. McGall, et al., Prop Natl Acad Sci USA (1996) 93:13555-60; and U.S. Pat. No. 6,040,138, all incorporated herein by reference. It is presently preferred to measure the genomic response by means of a nucleotide array, such as, for example, ~~GeneChip®~~ GENECHIP® probe microarrays (Affymetrix Inc., Santa Clara, Calif.), ~~CodeLink™~~ CODELINK™ ~~Bioarray~~ microarray (Motorola Life Sciences, now a product of Amersham Biosciences), and the like. Polynucleotide probes for interrogating the tissue or cell sample are preferably of sufficient length to specifically hybridize only to appropriate, complementary genes or transcripts. Typically, the polynucleotide probes will be at least 10, 12, 14, 16, 18, 20 or 25 nucleotides in length. In some cases, longer probes of at least 30, 40, 50 or 60 nucleotides will be desirable. The genes examined using the array can comprise all of the genes present in the organism, or a subset of sufficient size to distinguish the genomic expression modulation due to compounds to the degree of resolution and/or confidence desired. The method of the invention is also useful for determining the size of a sufficient subset of genes necessary for this purpose

Please amend paragraph 59 on pages 18-19;

[0059] ***Hybridization to Micorrays:*** 10 μg of fragmented cRNA was used for hybridization onto CODELINK™ microarrays (Motorola Life Sciences, now a product of Amersham Biosciences) using the protocol described in R. Ramakrishnan et al., Nuc. Acids Res (2002) 30:60. After an 18 hour hybridization at 37°C, the 12-slide shaker tray was removed from the ~~Innova™~~ INNOVA™ 4080 shaker tray, and the hybridization chamber taken off each slide. Each slide was placed into the BioArray Rack of the Parallel Processing Tool (Motorola Life Sciences, now a product of Amersham Biosciences) and incubated with 0.75x TNT (0.075 M Tris-HCI, pH 7.6, 0.1125 M NaCl, 0.0375% Tween-20®) at 46°C for 1 hour. The BioArray rack was moved from the reservoir containing TNT and transferred to a small reagent reservoir containing 1:500 dilution of streptavidin-Alexa 647 (Molecular Probes). The signal was developed for 30 minutes at room temperature, before the reaction was stopped and slides were washed four times for 5 minutes each in TNT buffer (0.1 M Tris-HC1, pH 7.6, 0.15 M NaC1, 0.05% Tween-20®) using a large reagent reservoir. The slides were rinsed in distilled, deionized water (dd-H_20) with 0.05% Tween-20® twice for 5 seconds each before they were dried by centrifugation and stored in light protective slide boxes.

Please amend paragraph 64 on page 21;

[0064] Various computer systems, typically comprising one or more microprocessors, can be used to store, retrieve, and analyze information obtained according to the methods of the invention. The computer systems can be as simple as a stand-alone computer having a form of data storage (i.e., a computer-readable medium, such as, for example, a floppy disk, a hard drive, removable disk storage such as a ZIP® drive, optical medium such as CD-ROM and DVD, magnetic tape, solid-state memory, magnetic bubble memory, and the like). Alternatively, the computer system can include a network comprising two or more computers linked together, for example through a network server. The network can comprise an intranet, an Internet

connection, or both. In one embodiment of the invention, a stand-alone computer system is provided with a computer-readable medium containing a Group Signature database thereon, said Group Signature database comprising one or more Group Signature records. The computer system preferably further comprises a processor and software that enables the system to compare gene expression and/or pharmacological data from an experiment with the contents of the Group Signature database. In another embodiment of the invention, a computer is provided with a computer-readable medium containing a Group Signature database thereon (a database server), and a network connection over which other computers can connect (user systems). Preferably, the user systems are provided with processors and software for receiving and storing gene expression and/or bioassay data from one or more experiments, and for formulating database queries for transmission over the network and execution on either the database server or on the user system. The computer system can further be linked to additional databases such as ~~Genbank™~~ GENBANK™ database (NCBI, Besthesda, MD)and ~~DrugMatrix™~~ DRUGMATRIX™ database (Iconix Pharmaceuticals, Inc., Mountain View, CA).